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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,842	06/18/2001	Stanley Stein	601-1-097 N	9975

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EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	7

DATE MAILED: 04/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/883,842	STEIN ET AL.	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Receipt of Applicant's amendment, filed on February 26, 2003, is acknowledged.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1 and 3-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (U.S. Patent 6,312,725) in view of Grinstaff et al. (U.S. Patent 5,498,421).

Wallace et al. discloses two-component polymer compositions useful for drug delivery, that react together to form a matrix at the site of administration, and teaches that both components have multiple functional groups (See col. 1, line 65 to col. 2, line 11). With respect to claims 4-12, Wallace et al. teaches that preferably both components are polymers, with the core of the polymer being polyethylene glycol (PEG), and the linkage formed between the two components may be a thioester, thioether or disulfide (See col. 2, lines 12-37). Wallace et al. provides a method of treating tissue for the purpose of drug delivery, comprising mixing the two components at the site of administration (See 2, line 55 to col. 3, line 4). With respect to claims 20-24 and 36, Wallace et al. includes ortho pyridyl disulfide in the presence of hydrogen peroxide, iodoacetamide, maleimides and vinylsulfones among the reagents used to facilitate bond formation (See col. 6, lines 41-67). With respect to the therapeutic agents claimed in claims

13 and 14, Wallace et al. includes optional materials in the compositions, such as proteins, drugs, cells and therapeutic agents, which may become covalently incorporated into the matrix, and teaches that preferably both components are liquid (See col. 7, line 61 to col. 8, line 50). The liquid formulations disclosed by the prior art contain buffer solutions, and thus comprise metal ions, as claimed in claims 17 and 18 (See col. 9, lines 12-36). Regarding claims 25-35, Wallace et al. teaches that the compositions of the invention can be locally administered using various methods and used in different pharmaceutical applications, in particular controlled release drug delivery (See col. 9, line 45 to col. 11, line 2).

Thus, Wallace et al. provides a two-component polymer composition that, when mixed together, reacts to form a matrix at the site of administration. Wallace et al. is deficient in the fact, that it does not specifically disclose an oil phase, as claimed in claims 1, 19, 28 and 37 and thus does not provide the compositions in the form of emulsion, as claimed in claim 3, and does not provide the kinetic profile of drug release from the compositions of the invention, as claimed in claims 15 and 16 of the instant application.

Grinstaff et al. provides compositions for in vivo delivery of solid or liquid active agents contained in crosslinked polymeric shells, through several routes of administration, including oral, subcutaneous, itraperitoneal and transdermal (See col. 7, line 60 to col. 8, line 33). Grinstaff et al. includes linear and branched PEGs among the synthetic polymers used in the invention, and teaches that the active agent may be dispersed in oil and the polymeric shells containing the active agent may be suspended in an aqueous medium to form lipid-containing emulsions (See col. 9, line 14 to col. 10, line 2). Grinstaff et al. teaches that the polymeric shell can be modified

by forming a covalent bond with crosslinked polymers, such as PEG derivatives, including PEG-thiols (See col. 12, line 14 to col. 13, line 27). Grinstaff et al. teaches that the compositions of the invention are suitable for delayed or controlled release of an entrapped pharmaceutical agent (See Example 5).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the compositions disclosed by Wallace et al., by providing said compositions in the form of emulsions, as taught by Grinstaff et al., to device controlled or delayed release compositions of drugs, which are insoluble in water. The expected result would have been a successful controlled release composition and successful methods of preparing, delivering or administering said compositions. Because of the teachings of Grinstaff et al., that water-insoluble drugs can be dispersed in oil and included in polymeric shells suspended in an aqueous phase, and the compositions are suitable for controlled or delayed release, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

1. Applicant's arguments, filed on February 26, 2003 have been fully considered but they are not persuasive.

2. Applicant argues that Grinstaff et al. provides polymeric shells and the combination of the prior art would yield biphasic emulsions encased in polymeric shells. Furthermore, Applicant argues that Grinstaff et al. teaches away from an emulsion not encased in a polymeric shell, because the art is intended to provide enhanced stability over emulsions. In response to said arguments, it is noted that the "comprising" language of the instant claims allows for the presence of polymeric shells, as disclosed by the prior art. With respect to the stability of the composition, the instant claims do not read on specific features, such as stability or lack thereof.

3. In response to Applicant's argument, that the crosslinking in the prior art takes place using functional groups in the polymeric shell, whereas the crosslinking in the invention utilizes functional groups present in the aqueous polymer in the aqueous phase, it is noted that the features upon which Applicant relies (i.e., crosslinking in the aqueous phase and the biophysical and biologic release properties of the oil phase, such as texture and elasticity) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

1. Claims 1 and 3-37 stand rejected.

2. Applicant's amendment has overcome the 35 U.S.C. 102(e) rejection of claims 1, 2, 4-7, 9, 11, 13, 14, 17-27, 29, 30, 34, 36 and 37 of the previous Office action, since the prior art does not teach an oil phase. Accordingly, said rejection is withdrawn.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

April 14, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600